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A review of analgesic medicinal plants in Iran

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ABSTRACT

Pain and inflammation are the main problems associated with different diseases in human communities. The currently available drugs including opioids and nonsteroidal anti-inflammatory drugs are helpful for all patients because of complications and side effects. Therefore, there is still the need for suitable analgesics and researchers are still studying in this regard. Medicinal plants are rich sources of bioactive substances and antioxidant, and could have analgesic uses. In this review study, analgesic medicinal plants were searched for. Medicinal plants and analgesics were used as key words. The findings indicated that Thymus vulgaris, Mentha pulegium, Ziziphora tenuior, Origanum vulgarel L.Spp, Satureja hortensis Linn, Salvia sclarea, Gundelia tournefortii L., Datura stramonium L., Carum copticum, Pistacia vera L., Coriandrium sativum, Cinnamomum zeylanicum,Artemisia herba-alba,Cuminum cyminum L., Elaeagnus angustifolia, Glycyrrhiza glabra, etc. are the most frequently used analgesics.

Key words: Medicinal plants, pain, drug mechanism, Iran

INTRODUCTION

Pain is a sensory unfavourite experience caused by acute or potential tissue damage. Pain is also a protective mechanism of the body to appropriately respond to eliminate pain-causing agent and an index for diagnosis of diseases [1].

Pain and inflammation are the main and basic problems associated with different illnesses in human communities. The currently available drugs including opioids, nonsteroidal anti-inflammatory drugs and some other agents could not be helpful for all patients because of complications and side effects [2]. Therefore, suitable analgesics are still required and researchers are still studying in this regard.

Severe pain results in fear and anxiety in patients and increased stress responses of hypothalamus through cortical stimulation. In addition anxiety and related stress responses cause increase in blood viscosity and platelet accumulation [3].

Analgesic drugs are categorized into opioids and non-opioids. Opioids exert their effect through connecting to central opioid receptors including μ, κ, and δ, that have central analgesic effect. Opioids include morphine, codeine, and heroine. Long term use of opioids results in physical tolerance and dependency and also increases the sensitivity to pain and hyperallergy [4].

Pain is developed by a variety of stimuli, including tissue mechanical pinching, low temperature, chemical substances (such as neural activator of pH released in injuries), and hyperosmotic solutions, with no commonality [5].

Given several pain-causing stimuli, the complexity of mechanisms of pain development, leading, and sensation, and that pain is the most prevalent clinical complaint of patients, biological sciences researchers worldwide are still seeking to find ways of overcoming pain, obviously resolving even a small question in this field could be an ointment for suffering patients.

Use of medicinal plants is one of the most primary ways of fighting diseases and relieving pain, and as pharmaceutical industry is advancing, many synthetic analgesics have been introduced into pharmacology with many side effects alongside promoting analgesic capacity [6].

Currently, the drugs used to relieve pain and decline inflammation are either narcotics such as opioids or non-narcotics such as salicylates and corticosteroids including hydrocortisone. All these drugs have well known toxic and side effects [7-9].

In the past decade, the interest in various types of complementary medicine has been increasing in patients, families, and healthcare professionals worldwide [10]. Because of potential side effects and inefficiency of chemical and synthetic drugs, application of complementary medications, particularly medicinal plants, for pain management is increasing [11].

The existence of hundreds of textbooks as available complete source of Iranian and Islamic medicine in Iran and the gift of cultivating various and occasionally rare medicinal plants in the world, Iran nation's interest in and cultural tendency toward native and Islamic medicine, side effects of chemical drugs, costly healthcare, no comprehensive treatment coverage of modern medicine for patients across Iran, defective and failed chemical healthcare system for treating patients, Iran's cultural and political dependency on other countries in medicine.

Decreased nationwide efficiency and community's health, a wide variety of diseases (diabetes, cholesterolemia, cardiac diseases, headache, allergy, depression, etc) and community's inability to treat them, and necessity of their persistent and costly control in community, and many other reasons including no inclusive perception of human personality by Allopathic have caused a tendency rapidly moving from Allopathic towards alternative medicine [12-17].

Most plant-derived drugs have been developed by studying traditional treatments and native knowledge of ancient ethnicities. Despite great advances in the science of synthetic compositions, some of the plant-derived drugs remain to be replaced with them [18-27]. Ethnobotany science is concerned with study of how the people of an ethnicity or community use plants, known as an efficient medium to generate native knowledge of how to use plants [28-34].

During the past decade, purposeful study of native pharmacopoeia aimed to develop new drugs has been entered into the scope of many national and international bodies. The positive attitude of scientists and increased tendency of governments toward cooperating with ethnobotany projects are indicative of the growing value of the data obtained from such studies [35-39]. Recording and study of written and non written knowledge of traditional medicine of various ethnicities in Iran leads to preserving the valuable treasure of Iran's medical sciences and experiences gathered throughout thousands of years, discovering new drugs, and advancing pharmaceutical industry [36-42]. This review study was conducted to study and identify Iran native medicinal plants with analgesic effect.

For this study, various combinations of words "*medicinal plants*", "*analgesic*", and "*Iran*" and their Persian equivalents were entered into various databases including Magiran, SID, and IranMedex as well as international databases of Web of Science, Pubmed, Scopus and Google Scholar. The articles in English and Persian languages published between 1976 and March, 2015 were considered in this study. Twenty three articles were included in the final analysis (Figure 1).

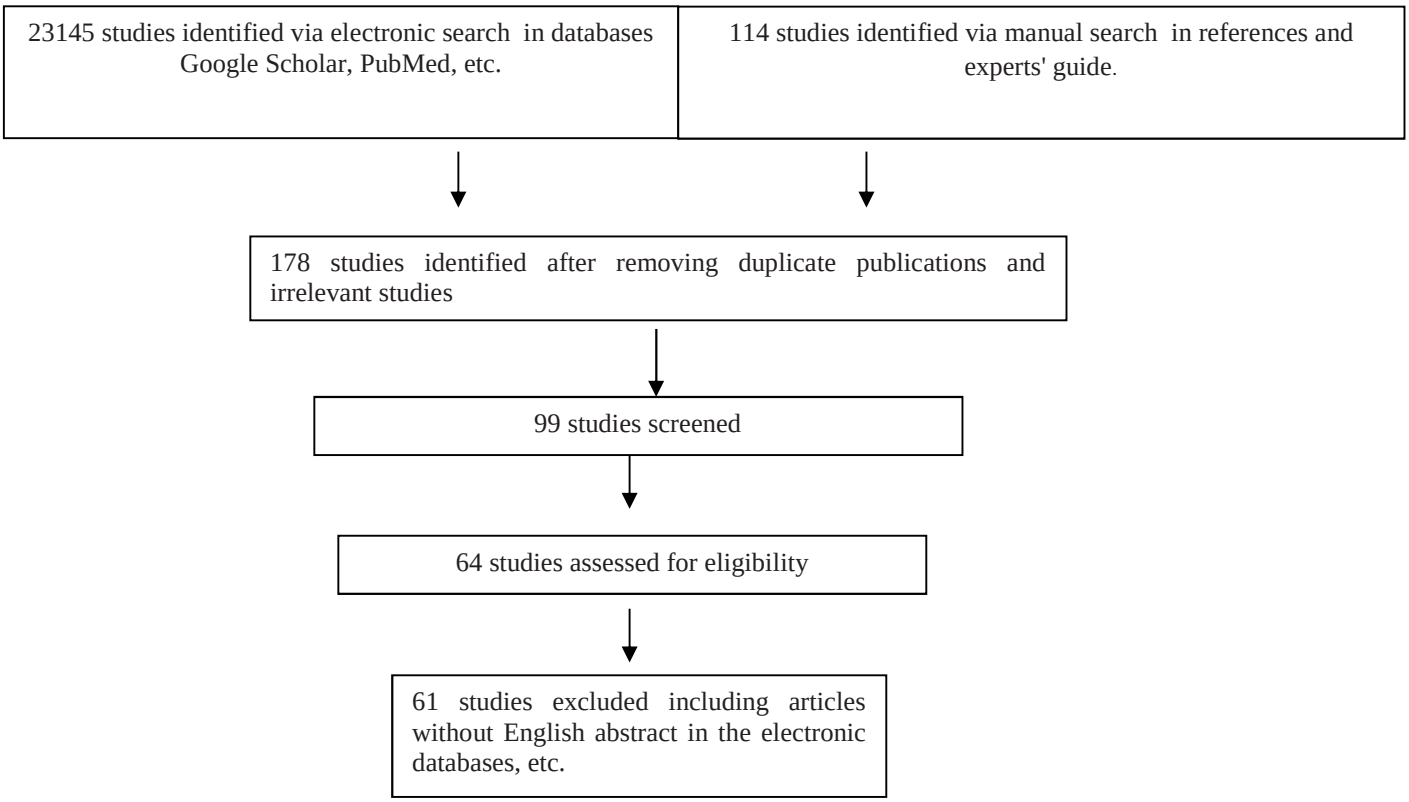

Figure. Flow diagram for the study review

RESULTS

The data of this review article indicated that 56 medicinal plants from 31 families in Iran are used as analgesic. Figure indicates that most (25%) plants with analgesic application in Iran are from Laminaceae family.

Table. Iran native analgesic medicinal plants and their scientific name, analgesic test, fraction, effect mechanism, and family

No	Plant name	Scientific name	Mechanism	Family	References
1	Ben sorkh	*Allium jesdanum*	Central analgesic activities and effect on opioid receptors	Lilaceae	[43]
2	Karafs	*Apium graveolens*	Inhibition of cyclo-oxygenase	Umbelliferae	[44]
3	Tarkhoun	*Artemisia dracunculus*	Presence of flavonoids and substances with benzodiazepines property	Asteraceae	[45]
4	Dermaneh	*Artemisia herba alba*	Stimulation of GABA A receptors	Artemisia	[46]
5	Dermaneh dashti	*Artemisia siberi Besser*	Inhibition of calcium release, blocking of receptor, TRPA1, inhibition of synthesis of NO, cytokines, and prostaglandin E2	Artemisia	[47]
6	Zereshk	*Berberis vulgaris L.*	Opioid system	Berberidaceae	[48]
7	Zenyan	*Carum copticum*	Effect of essential fatty acids	Umbelliferae	[49]
8	Darchin	*Cinnamomum zeylanicum*	Inhibition of NO synthesis, inhibition of TNF and COX2, inhibition of prostaglandins, and stimulation of opioids receptors	Lauraceae	[50]
9	Gole hasrate-barfi	*Colchicum szovitsii Fisch& C.A.Mey*	Anti-inflammatory effects and opioid pathways	Colchicaceae	[51]
10	Geshniz	*Coriandrium sativum*	-	Verbenaceae	[52]
11	Zaefaran	*Crocus sativus*	Potential inhibition of NMDA receptors and NO synthesis	Iridaceae	[53]
12	Zireh sabz	*Cuminum cyminum L.*	-	Apiaceae	[54]
13	Tatoureh	*Datura stramonium L.*	Strengthening of opioid system and decrease of peripheral and central pain-causing mediators	Solanaceae	[55]
14	Bilhar	*Dorema aucheri*	Inhibition of synthesis of NO and NMDA receptors and stimulation of opioid and adrenergic system	Umbelliferae	[56]
15	Shabnam khorshid	*Drosera spatulata*	Activity of **nucleus paragigantocellularis**	Droseraceae	[57]
16	senjed	*Elaeagnus angustifolia*	Inhibition of proinflammatory mediators and NMDA receptors	Elaeagnacea	[58,59]
17	Shirmal	*Euphorbia helioscopia*	Effect of flavonoids and steroids	Euphorbiaceae	[60]
18	Razianeh	*Foeniculum vulgare*	Serotonergic and histaminergic receptors	Apiaceae	[61]
19	Glosium	*Glaucium grandiflorum*	Alkaloids	Papaveraceae	[62]
20	Shirin bayan	*Glycyrrhiza glabra*	Inhibition of white blood cells migration and production of inflammatory mediators in neutrophils	Fabaceae	[63]
21	Kangar	*Gundelia tournefortii L.*	Serotonergic, gabanergic, and adrenergic and inflammatory processes	Asteraceae	[64]
22	Razak	*Humulus lupulus L.*	Opioid receptors	Cannabaceae	[65,66]
23	Nang dane	*Hyoscyamus niger*	Cholinergic and opioid mechanisms	Solanaceae	[67]
24	Alafe chay	*Hypericum perforatum*	Inhibition of COX1 and 5-LO enzymes	Hypericaceae	[68]
25	Gerdou	*Juglans regia*	Inhibition of COX1 enzyme, inhibition of calcium release, cholinergic,	Juglandaceae	[69]

			histaminergic, and adrenergic mechanisms		
26	Kahouye irani	*Lactuca sativa longifolia*	Central and peripheral mechanisms	Comositeae	[70]
27	Ostokhodous	*Lavandula officinalis*	Effect on inflammatory processes	Lamiaceae	[71]
28	Babouneh	*Matricaria chamomilla*	Colinergic mechanisms	Asteraceae	[72]
29	Babaouneh	*Matricaria chamomilla*	Inflammatory processes	Comositeae	[73]
30	Nakhonak	*Melilotus officinalis*	Inflammatory and opioid effects-free processes	Leguminosae	[74]
31	Badranjbouye	*Melissa officinalis*	Analgesic central mechanism	Lamiaceae	[75]
32	Naena	*Mentha piperita Linn*	Central and peripheral effects	Lamiaceae	[76]
33	Poune	*Menthe pulegium*	Inhibition of synthesis of NO and inflammatory mediators and NMDA receptors and stimulation of opioid receptors	Lamiaceae	[77]
34	Marzanjoush	*Origanum vulgarel L.spp viride*	Antioxidant compounds and inflammatory processes and opioid receptors	Lamiaceae	[78,79]
35	Jafari	*Petroselinum crispum L.*	Activation of analgesic pathways	Umbelliferae	[80]
36	Khorma	*Phoenix dactylfera*	Increase in blood carbohydrates and increase in the level of beta-androphines and peripheral mechanisms	Palmaceae	[81]
37	Felfele siah	*Piper nigurm*	Anti-inflammatory and central	Piperaceae	[82]
38	Pesteh	*Pistacia vera L.*	Inhibition of opioid receptors and inhibition of inflammatory mediators	Anacardiaceae	[83]
39	Khorfeh	*Portulaca oleracea*	Central and peripheral effects	Portulacaceae	[84]
40	Gole mohammadi	*Rosa demascena*	Opioid system	Rosaceae	[85]
41	-	*Saliva hydrangea*	Inhibition of synthesis pathway of prostaglandins	Lamiaceae	[86]
42	-	*Salvia hypoleuca*	Opioid system and inhibition of proinflammatory mediators	Lamiaceae	[87]
43	Maryam goli	*Salvia sclarea*	Peripheral effectd and inflammatory processes and opioid receptors	Lamiaceae	[88,89]
44	-	*Sambucus ebulus*	Inhibition of prostaglandins inhibition	Adoxaceae	[90]
45	Marzeh	*Satureja hortensis linn*	Through central mechanisms and inflammatory processes	Lamiaceae	[91]
46	Gande talkhe	*Securigera securidaca L.*	Inhibition of synthesis of NO and COX2	Papilionaceae	[92]
47	Bademjan	*Solanum melongena*	Peripheral analgesic mechanism and cholinergic pathways	Solanaceae	[93]
48	Azarchoub	*Solenanthus circinnatus*	Through inhibition of central and peripheral pathways	Boraginaceae	[94]
49	Chaye kouhi	*Stachys Lavandulifolia*	Inhibition of cyclo-oxygenase	Lamiaceae	[95]
50	Mokhalase	*Tanacetum parthenium*	Inflammatory processes	Asteraceae	[96]
51	Maryamnokhodi khazari	*Teucrium hyrcanicum*	Inhibition of prostaglandins synthesis and inhibition of central nervous system	Lamiaceae	[97]
52	Kalpoure	*Teucrium polium*	Connecting to pain receptors and affecting ligand-sensitive channels and decreasing sodium entry	Lamiaceae	[98]
53	Avishan	*Thymus vulgaris*	-	Lamiaceae	[99]
54	Shanbalileh	*Trigonella foenum graecum*	Effect of serotonergic system	Apiaceae	[100]
55	Zanjabil	*Zingiber oficinalis*	Inhibition of release of peripheral mediators, cytokine, TNF, and interleukin 1β, nuclear factor κB	Zingiberaceae	[101]
56	Kakouti	*Ziziphora tenuior*	Inhibition of arachidonic acid release and synthesis of prostaglandins and effect on opioid system	Lamiaceae	[102]

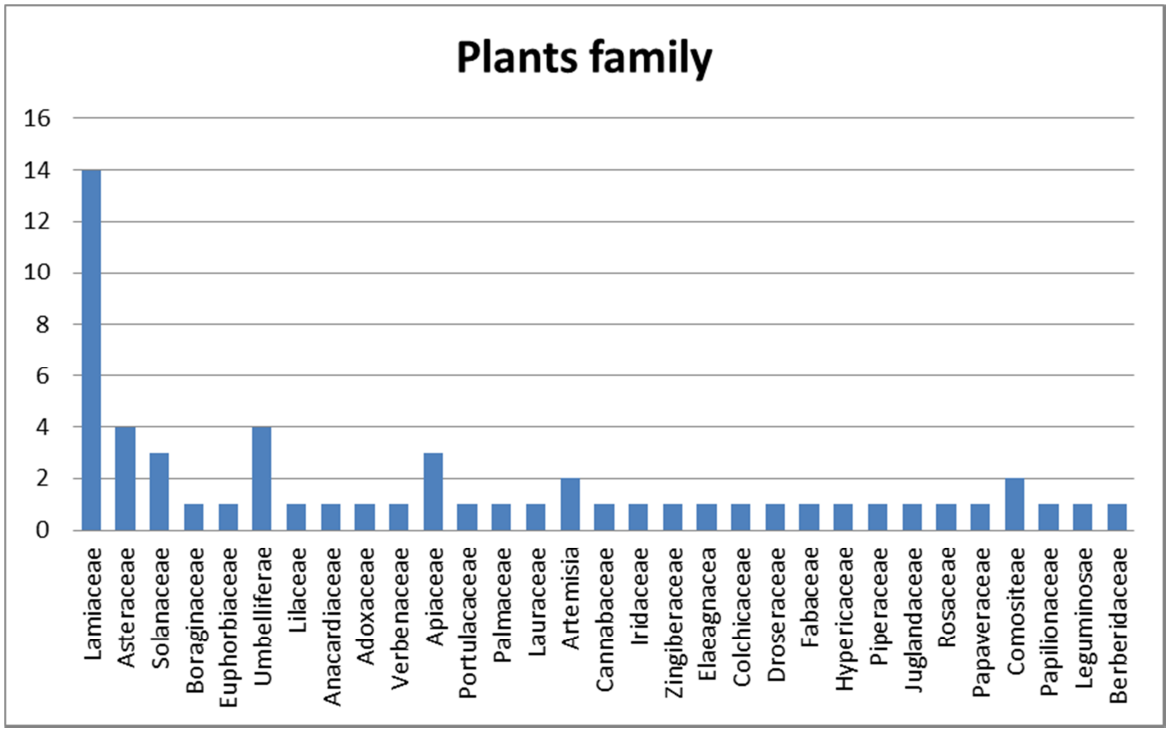

Figure 1: Family herbs

The data of this review article indicated that 56 medicinal plants from 31 families in Iran are used as analgesic, 25% of which are from Laminaceae family. The medicinal plants from Laminaceae family seem to have biological compounds and compositions that exert analgesic effect.

DISCUSSION

Diseases, inflammation, and damage to peripheral and central nervous system cause obvious changes in pain pathways such as increase in stimulation and change in expression of genes and new molecules such as neurotransmitters, enzymes, and receptors. Certain pains in long term cause mental and psychological adverse effects. Therefore, human has been always seeking for a solution to remove or relieve pain [96].

As Table 1 shows, the highest analgesic test in this study was formalin test (51%). Formalin analgesic test has two steps, acute and chronic. Acute step is related to neurogenic pains, throughout which the message of pain is transmitted through specific neural routes.

Chronic step is related to inflammatory pains, throughout which the message of pain is transmitted because of the inflammatory reaction caused by formalin administration. The drugs that are likely to affect nervous system usually affect the acute step, as well, and anti-inflammatory drugs lead to moderating pain often in chronic step [62].

Given the obtained findings in this review article, it could be concluded that among plant species with analgesic property, most plant species were from Laminaceae family and among different analgesic compounds, phenolic compounds particularly flavonoids have been largely considered.

Further, terpenes and essential and volatile oils have analgesic oils, as well. These phenolic compounds are present in most of the above plants. Most phenolic compounds have antioxidant property [103-115]. Since pain is mainly associated with increased oxidative stress, these plants also can exert their analgesic effect through this way.

However there are many other plants with antioxidant effect [116-126].

Nowadays, different diseases are highly increasing in prevalence and spreading because of living conditions and environment, diet, weather, stress, bad food habits, mechanical life, etc. Remedies of this disorders and diseases is very important[127-161].As a result, this class of plants could also have analgesic effect and should be studied. Iran is a rich source of medicinal plants, and paying attention to and preserving them as a national asset could contribute significantly to the nation's development.

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